IN THE UNITED STATES DISTRICT COURT FOR THE WESTERN DISTRICT OF TENNESSEE WESTERN DIVISION

PATRICIA NOZINICH and PETER NOZINICH,	§	
Plaintiffs,	§	
vs.	§	**Case No. 2:09-cv-02105-dkv**
JOHNSON & JOHNSON, INC., and CENTOCOR ORTHO BIOTECH, INC.,	§	**Jury Demand**
Defendants.	§	

PLAINTIFFS' RESPONSE TO DEFENDANTS' STATEMENT OF UNDISPUTED MATERIAL FACTS IN SUPPORT OF DEFENDANTS' MOTION FOR SUMMARY JUDGMENT

A. **Remicade ®**

1. Remicade ® is a prescription biologic, which was approved for marketing by the United States Food and Drug Administration ("FDA") in August 1998 for the treatment of Crohn's disease and in November 1999 for the treatment of rheumatoid arthritis. (Affidavit of Stella Jones, PhD ("Jones Aff."), Dkt. Entry No. 83, ¶¶ 4,5.)

Undisputed.

2. Remicade ® has been specifically approved for a number of indications, including, in combination with methotrexate, reducing signs and symptoms, inhibiting the progression of structural damage and improving physical function of patients with moderately to severely active rheumatoid arthritis. (*Id.*, ¶ 3(I).)

Undisputed for the purpose of ruling on the summary judgment motion only.

3. In approving Remicade ® for the treatment of rheumatoid arthritis, FDA rigorously evaluated and scrutinized the medicine and concluded that Remicade ® is safe and effective and that its benefits outweigh its risks. (*Id.*, ¶¶ 2,5.)

Disputed.

Neither paragraphs two nor five of Stella Jones' affidavit state that the FDA "rigorously evaluated" or "scrutinized" the safety of Remicade. (Ex. 1 - Stella Jones' Aff. ¶¶ 2, 5). Rather, the facts show that the FDA did not rigorously evaluate or scrutinize the medicine because the clinical trial on which the FDA relied on for approval were, ACCENT I & II and ATTRACT I & II, biased in favor of FDA approval because they were sponsored by the defendants, the makers of Remicade. (Ex. 2 - Letter from Centocor to Dr. Ash dated February 28, 2008). Further, the defendants as the sponsors of the clinical trials on which the FDA relied were responsible for supplying the safety information and presenting it to the FDA in order to obtain approval for various indications. (Ex. 3 - Barbara Matthews' Goldstein depo. p. 41). Dr. Matthews, who was the FDA medical officer who reviewed the clinical trials for Remicade's investigated new drug applications, admitted that the number of subjects in the pre-approval clinical trials was too low to pick up all of the adverse events that may be associated with Remicade. (Collective Ex. 4 - Barbara Matthews' Ervin depo. p. 52–53). Furthermore, the credibility of Dr. Matthews is suspect because first her employment with the defendants and now her contract status with Johnson & Johnson, Inc. (Ex. 5 - Barbara Matthews' depo. p. 15-16).

4. Since its approval in 1998, FDA has reaffirmed the safety and efficacy of Remicade ® on more than fifteen occasions. (*Id.*,¶ 5.).

Disputed.

Since Remicade's approval in 1998, the FDA has instructed the defendants to issue multiple black box warnings and multiple "dear doctor" letters warning of the dangers and risks of associated with taking Remicade. (Ex. 6 – Warnings)

5. Both before and after Remicade ® was approved for the treatment of rheumatoid arthritis by FDA studies were conducted to assess the safety of the medicine. The occurrence of thrombotic events, including pulmonary embolism, in patients being treated for rheumatoid arthritis were part of these studies. When data from these studies was evaluated, it was determined that the incidences of pulmonary embolism amongst Rheumatoid Arthritis patients is 0.197%. (*Id.*,¶ 10.)

Disputed.

The first paragraph numbered ten (10) of Stella Jones' affidavit states that the incident rate for thromboembolic events from 1998–2008 was 0.065%. (Ex. 1 - Stella Jones' Aff. ¶ 10). The second paragraph numbered ten (10) makes no reference to rate of incidence of pulmonary embolism among rheumatoid arthritis patients. (Ex. 1 - Stella Jones' Aff. ¶ 10).

The defendants' numbers do not add up. In paragraph 5 above, the defendants claim that the rate of incidence of pulmonary embolism among rheumatoid arthritis patients is 0.197%. However, Stella Jones swears in her affidavit that total rate of thromboembolic events among all patients taking Remicade during this time is 0.065%. (Ex. 1 - Stella Jones Aff. ¶ 10). Thus, according to the defendants' statement of facts the rate of incidence is higher in a subgroup of a subgroup, (i.e., patients with

rheumatoid arthritis who suffered a pulmonary emboli) than all patients taking Remicade who experience some type of thromboembolic event. (See id.).

Barbara Matthews, who was the medical investigator for Remicade, testified that the defendants did not perform safety studies in pre-approval clinical studies. (Collective Ex. 4 - Barbara Matthews' Ervin depo. p. 226). Thus, the safety of Remicade was not tested before the FDA approved Remicade. Rather, the studies conducted tested efficacy. (Id.). The safety studies which have been performed are on-going, and therefore inconclusive. (Collective Ex. 7 – Suzanne Travers depo. p. 211-212).

6. Pulmonary embolism was listed as an adverse event in the Remicade ® package insert beginning in 1999. (Id. ¶ 9.)

Disputed.

Stella Jones' affidavit contains two paragraphs numbered nine. The second paragraph 9 of Stella Jones' affidavit states that pulmonary embolism was listed as an adverse even in the Remicade package insert beginning in 2001–2009, not beginning in 1999. (Ex. 1 - Affidavit of Stella Jones ¶ 9). The first paragraph numbered nine does not address when the defendants began listing pulmonary embolism as an adverse event. (Ex. 1 - Affidavit of Stella Jones ¶ 9).

7. The prescribing physician in this case, Dr. Judy Ash, testified that she was aware of this information and, because the occurrence of pulmonary embolism was so low in patients being treated with Remicade ®, she decided not to share this information with Ms. Nozinich prior to treating her rheumatoid arthritis with Remicade ®. (*See*

November 30, 2010 Deposition of Judy D. Ash, M.D. ("Ash Dep."), 36:6-24) (excerpts of Ash Dep. attached collectively hereto as **Ex. A**).

Disputed.

Dr. Ash only received the defendants' out dated clinical trial data which stated that thrombophlebitis and pulmonary embolism were among those incidences that occurred at a rate equal to placebo rate. (Collective Ex. 8 - Dr. Ash depo. p. 36). Due to the very low percentage rate provided to Dr. Ash by the defendants, Dr. Ash did not consider pulmonary embolism a clinically significant event. (Collective Ex. 8 - Dr. Ash depo. p. 36). After Ms. Nozinich was hospitalized for pulmonary emboli, Dr. Ash also would have liked to have seen the Periodic Safety Updates (PSUR's) and data containing post marketing numbers before continuing to prescribe Remicade to Ms. Nozinich. (Collective Ex. 8 - Dr. Ash depo. p. 36). Additionally, Dr. Trew points out that the rate of incidence should be based on thromboembolic events as a whole and not pulmonary embolism event specifically. (Collective Ex. 9 - Dr. Trew depo. p. 42-43). Had this been done, the rate of incidents would have been higher and would have more accurately identified the risk of all thromboembolic events. (Collective Ex. 9 - Dr. Trew depo. p. 42-43).

8. In April 2010, FDA approved the removal of pulmonary embolism as an adverse event from the Remicade ® package insert, in compliance with FDA's guidance document for labeling of the adverse events section. More specifically, after considering the necessary factors- seriousness of the event, number of adverse event reports and strength of the causal relationship to the medication – FDA concluded that

pulmonary embolism no longer met the necessary criteria to be included as an adverse event in the prescribing information for Remicade® (Id., ¶¶ 10, 11.)[1]

Disputed. The plaintiffs do not dispute the first sentence of paragraph 8. To the extent that the statement asserts that the FDA or the defendants considered the necessary factors for removing the warning against pulmonary embolism, the plaintiffs dispute that this factually accurate because the defendants originally removed the warning label in 2002 and replaced by 2004. (Ex. 10 - Copy of 2002 Remicade Package Insert) (Ex. 11 - Copy of 2004 Remicade Package Insert). Furthermore, any evidence of post incident changes to the label is irrelevant; therefore, inadmissible. Fed. R. Evid. 401, 402, & 403.

B. Patricia Nozinich's Relevant Medical History

9. Ms. Nozinich was diagnosed with rheumatoid arthritis in April 2004. (Ash Dep. at 13:5-23.)

Undisputed.

10. Ms. Nozinich has a body mass index of 33.8, which classifies her as obese, and she has hyperlipidemia. (Affidavit of Dr. Gary Epler ("Epler Aff."), Dkt. Entry No. 84, ¶ 8; March 7, 2011 Deposition of Dr. Gary F. Trew ("Trew Dep."), 72:21-24) (excerpts of Trew Dep. attached collectively hereto as **Ex. B**).

Undisputed.

11. Prior to being treated with Remicade ®, Dr. Ash treated Ms. Nozinich's rheumatoid arthritis with several medications: Plaquenil®, Bextra®, Enbrel ®, Mobic ®,

[1] The Statement of Fact originally filed by the defendants on April 7, 2011 was incomplete. The defendants filed a complete Statement of Facts on May 4, 2011. The plaintiffs have used the complete Statement of Facts in their response.

Celebrex ®, Methotrexate, and Arava®. (Ash Dep. At 14:10-12; 15:1-3, 17-20; 17:9-17; 187-10.)

Undisputed.

12. At the recommendation of Dr. Ash, Ms. Nozinich began Remicade ® treatments on October 30, 2007 to alleviate the symptoms of her rheumatoid arthritis. (*Id*. At 22:9-14.)

Disputed. Ms. Nozinich based her decision to take Remicade infusions on her discussion with Dr. Ash as well as her review of the promotional brochure and DVD produced by Centocor which contained no warning of pulmonary embolism. (Collective Ex. 12 – Patricia Nozinich depo. p. 54).

13. Ms. Nozinich received her Remicade ® infusions on October 30, 2007, November 27, 2007; and December 16, 2007. (Epler Aff., ¶ 11.)

Undisputed.

14. While being treated with Remicade ®, Ms. Nozinich was still being treated with Celebrex ®, and methotrexate, both of which have an associated risk of pulmonary embolism. (Trew Dep. at 72:9-24.)

Undisputed.

15. In November 2007, Ms. Nozinich and her husband drove from Coldwater, Mississippi to Pittsburgh, Pennsylvania to attend a funeral. (February 22, 2010 Deposition of Patricia Nozinich ("Nozinich Dep.), 69:10-70.9) (excerpts of Nozinich Dep. attached collectively hereto as **Ex. C**). The automobile ride took fifteen hours each way, and they made the trip in a span of two days. (Id.)[2]

[2] The Statement of Facts originally filed by the defendants ended without a complete list of citations to the record upon which the defendants were relying on (D.E. No. 86-6). On May 4, 2011, the defendants provided the plaintiffs

Disputed. To the extent that the statement implies that the plaintiffs drove directly from Coldwater, Mississippi to Pittsburg, Pennsylvania without stopping, the statement is factually incorrect. (Collective Ex. 13 - Peter Nozinich depo. p. 31-32).

16. During the trip to Pittsburg, Ms. Nozinich began experiencing chest pain and had difficulty breathing (Nozinich Dep. at 69:10-70.9; Deposition of Peter Nozinich ("Peter Nozinich Dep.") at 31:3-32:9) (excerpts of Peter Nozinich Dep. attached collectively hereto as **Ex. D**)

Disputed. Ms. Nozinich began experiencing chest pain and difficulty breathing following her first Remicade infusion, which occurred on October 30, 2007. (Collective Ex. 12 - Patricia Nozinich depo. at 69:4) (Collective Ex. 13 - Peter Nozinich dep. at 30:18-24). The trip to Pittsburgh, Pennsylvania took place during November 2007. (Collective Ex. 12 - Patricia Nozinich depo. at 69:10–70:9) (Collective Ex. 13 - Peter Nozinich depo. at 31:3–32:9).

17. On January 15, 2008, Ms. Nozinich was hospitalized at Baptist Hospital because of a productive cough and associated shortness of breath, and suffered a pulmonary embolism. (Ash Dep. at 48:15-19.)

Disputed. Ms. Nozinich began experiencing extreme chest pain and shortness of breath on January 15, 2008. (Ex. 14 - Baptist Memorial Hospital Discharge Summary Record dated January 21, 2008). She went to Baptist Hospital and was diagnosed as having multiple pulmonary emboli in both lungs. (Ex. 15 - Epler Aff., ¶ 6.)

18. While in the hospital, Dr. Gary F. Trew used the drug Coumadin to treat Ms. Nozinich for her pulmonary embolism. (Epler Aff., ¶ 6.)

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with a complete copy of their Statement of Facts. The plaintiffs have used the complete copy of the defendants Statement of Facts in their response.

Undisputed.

19. On February 19, 2008, Ms. Nozinich received her fourth Remicade ® infusion. (Epler Aff., ¶ 11.)

Undisputed.

20. Dr. Ash testified that prior to her fourth Remicade ® infusion, she knew Ms. Nozinich had experienced a pulmonary embolism, but Dr. Ash went ahead with the infusion because Dr. Ash did not think the embolism was related to Remicade ® or, more particularly, that Remicade ® was the cause because the risk of pulmonary embolism associated with Remicade ® was very low. (Ash Dep. at 49:21-24; 50:1-16.)

Disputed. The reported information that the defendants provided to Dr. Ash in 2006 showed that the risk of pulmonary embolism associated with Remicade was equal to placebo, but the defendants' did not provide Dr. Ash with complete information regarding the risk of pulmonary embolism associated with Remicade. (Collective Ex. 8 – Dr. Ash depo. p. 36).

21. While being treated with Remicade ®, Ms. Nozinich's rheumatoid arthritis improved. (*See Id.* at 50:10-16.)

Undisputed.

22. According to Dr. Trew, Ms. Nozinich's obesity, rheumatoid arthritis, hyperlipidemia and fifteen hour automobile ride put her at an increased risk for, or predisposed her to, developing blood clots that could result in a pulmonary embolism. (Trew Dep. at 69:3-25; 88:17-89:4; 129:4-130:2.)

Disputed. Dr. Trew testified that obesity, rheumatoid arthritis, and hyperlipidemia carry a risk of pulmonary embolism. (Collective Ex. 9 – Dr. Trew depo. p. 72-73).

23. According to Drs. Trew and Ash, Embrel®, Bextra®, Celebrex®, and methotrexate also put her at an increased risk for, or predisposed her to, developing blood clots that could result in pulmonary embolism. (*See Id*; Ash Dep. at 68:16-69:16.)

Disputed. Dr. Trew testified that these drugs carried a risk of pulmonary embolism, but appropriately ruled out that they caused Ms. Nozinich's pulmonary emboli. (Collective Ex. 9 – Dr. Trew depo. p. 72-73).

C. Dr. Ash's Knowledge and Understanding about Remicade ®

24. Dr. Ash began prescribing and infusing Remicade ® prior to the year 2003. November 30, 2010 30(b)(6) Examination of The Rheumatology and Osteoporosis Center of Memphis - Richard Timothy Wallace ("Wallace Dep."), 75:6-16) (excerpts of Wallace Dep. attached collectively hereto as **Ex. E**)

Undisputed.

25. Based on their knowledge and experience with Remicade ®, in 2003, Dr. Ash, her fellow physicians and the Board of Directors of The Rheumatology and Osteoporosis Center of Memphis made the decision to start doing Remicade ® infusions onsite at their facilities in 2003. *See Id.*

Disputed. Centocor provided the Rheumatology and Osteoporosis Center of Memphis with education information about in-clinic Remicade infusions, materials to address the practice's current business issues and Medicare Billing. (Ex. 16 – June 21, 2010 Deposition of Therese Despeaux depo. p. 52-53, 63-64).

26. Dr. Ash was aware of the reports of pulmonary embolism and the reports of thromboembolic events associated with Remicade ® at the time she began doing

onsite Remicade® infusions in 2003 and at the time she prescribed the medicine to Ms. Nozinich in 2007. (Dr. Ash Dep. 35:22-36:19; 68:1-5.)

Disputed. Dr. Ash was aware of the outdated rate of incidence reported in the package insert for use of Remicade, which describes pulmonary embolism as a rare but possible side effect. (Collective Ex. 8 - Dr. Ash depo. p. 36). She was not provided current post-marketing information related to all thromboembolic events by defendants that was readily available to defendants by intentionally withheld.

27. Based on her knowledge of and experience with Remicade®, Dr. Ash exercised her independent clinical judgment in prescribing the medicine to Ms. Nozinich to alleviate the symptoms of her rheumatoid arthritis. (*Id.* 36:20-24.)

Disputed. Dr. Ash relied solely on the outdated information provided to her by the defendants regarding the possible side effects of Remicade. (Collective Ex. 8 - Dr. Ash depo. at 35:22 – 36:24). The information that the defendants provided to Dr. Ash was incomplete and did not fully apprise her of the risks of thromboembolic events associated with Remicade. (Collective Ex. 8 - Dr. Ash depo. at 36:13).

28. Remicade® was prescribed properly to Ms. Nozinich by Dr. Ash and she was benefitting from the medicine as the symptoms of her disease were improving after the infusions. (*See* Ash Dep. at 14-22; Nozinich Dep. at 66:7-19; 77:10-78:5; 79:5-8)

Disputed. Dr. Ash prescribed Remicade to Ms. Nozinich based on the information that the defendants' provided to Dr. Ash. (Collective Ex. 8 – Dr. Ash depo. p. 22, 31). Ms. Nozinich suffered multiple, debilitating pulmonary emboli as a result of taking Remicade and can no longer take currently available rheumatoid arthritis treatments because of the fatal risk associated with future thromboembolic events.

(Collective Ex. 8 – Dr. Ash depo. p. 65) (Collective Ex. 12 – Patricia Nozinich depo. p. 115-116).

29. Dr. Ash did not actually rely on any representations or alleged concealments made by Centocor when prescribing Remicade ® to Ms. Nozinich. Rather, Dr. Ash, who already was familiar with Remicade ® from her prior experience with and research of the drug, recommended it to Ms. Nozinich because she was not responding to her current medications and believed that Remicade ® may help Ms. Nozinich. (Ash depo. at 35:22-36:19.)

Disputed. Dr. Ash relied on information she requested from the defendants to make the clinical decision to prescribe Remicade to her patients. (Collective Ex. 8 – Dr. Ash depo. p. 36). She requested specific information on behalf of another patient before prescribing Remicade to Ms. Nozinich and was provided only the results of the outdated pre-marketing studies. (Collective Ex. 8 – Dr. Ash depo. p. 36). No post-marketing reports such as PSURs were provided. (Collective Ex. 8 – Dr. Ash depo. p. 54). After Ms. Nozinich was diagnosed as suffering from pulmonary emboli, Dr. Ash again requested additional information from the defendants regarding the link between Remicade and pulmonary embolism. (Collective Ex. 8 – Dr. Ash depo p. 39-40). She was again provided limited non-current information. (Collective Ex. 8 – Dr. Ash depo p. 39-40). She relied on the incomplete information that the defendants provided to continue to prescribe Remicade to Dr. Ash after Ms. Nozinich was originally diagnosed with pulmonary emboli. (Collective Ex. 8 – Dr. Ash depo. at 37:1)

30. Dr. Ash was not influenced at any seminars, presentations, or through literature provided by Centocor regarding Remicade ®. To the contrary, plaintiff's

evidence is that Dr. Ash is the type of good doctor who would never compromise on patient safety and would only prescribe a medicine if it was in her patient's best interests. (*See Id.*; Trew Dep. at 36:15-38:7; 115:1-116:8).

Plaintiffs **dispute** the first sentence. The second sentence is **undisputed**. Dr. Ash relied on the outdated literature Centocor provided to her regarding the link between pulmonary embolism and Remicade when she originally prescribe Remicade to Ms. Nozinich and again when she continued the Remicade infusions after Ms. Nozinich was diagnosed with pulmonary emboli. (Collective Ex. 8 – Dr. Ash depo. p. 36-40).

31. Dr. Ash used her own independent medical judgment to decide whether to prescribe Remicade ® to Ms. Nozinich, as well as to determine what information to provide Ms. Nozinich. (Ash Dep. 35:22-36-24; 41: 1-17; 68:1-5.)

Disputed. Dr. Ash relied on the incomplete outdated information that the defendants provided to her regarding the causal relationship between pulmonary embolism and Remicade. (Collective Ex. 8 – Dr. Ash depo. p. 39-40).

D. <u>Defendant's Status</u>

28. Johnson & Johnson ("J&J") is a company incorporated under the laws of the state of New Jersey, with its principal place of business in New Brunswick, New Jersey. J&J is a shareholder of companies providing health care products and services. Each of these companies operates independently of J&J. (Affidavit of Lacy Elberg ("Elberg Aff."), Dkt. Entry No. 82 ¶3.)

The first and second sentences are **undisputed**. The third sentence is **disputed**. Employees of Centocor work for J & J. (Ex. 16 – June 21, 2010 Deposition

of Therese Despeaux depo. p. 31). Employees of J & J also work for Centocor. (Collective Ex. 7 Travers depo. p. 12).

29. Centocor was a wholly-owned subsidiary of J&J, and was a corporation organized and existing under the laws of the state of Pennsylvania. (*Id.*, ¶ 4.)

Undisputed.

30. J&J does not manufacture, market, sell, or distribute any products. More specifically, J&J did not design and does not manufacture, inspect, advertise, distribute, and/or sell Remicade ®. Any such activities were conducted prior to December 31, 2009 independently by Centocor in relation to Remicade ®. (*Id.*, ¶ 5.)[3]

Disputed. J & J sells and markets Remicade through its employee agents. (Ex. 16 – June 21, 2010 Deposition of Therese Despeaux depo. p. 31).

31. J&J and Centocor managed and operated their own day to day business activities independently of one another. J&J and Centocor maintained their own boards or directors and officers, who are primarily responsible for their respective business. J&J and Centocor were completely separate legal entities, and their only corporate relationship were ones of parent-subsidiary. (Id., ¶ 6.)

Disputed. Centocor holds the rights to Remicade, but the safety database SCEPTER for Remicade is controlled, managed and maintained by J & J. (Collective Ex. 7 - Travers depo. p. 28-29).

32. The separate corporate identities of each legal entity have been maintained. Centocor was not a shell or sham corporation of J&J. Likewise, J&J is not a shell or sham corporation of Centocor. (Id., ¶ 11.)

[3] The Statement of Facts filed by the defendants on April 7, 2011 (D.E. No. 86-6) was incomplete and ended here. On May 4, 2011, the defendants provided the plaintiffs with a complete Statement of Facts. The plaintiffs used the complete Statement of Facts for their response.

Undisputed for purposes of ruling on the motion for summary judgment.

Respectfully submitted,

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that he is attorney of record for the plaintiff and that he has served a true and correct copy of the foregoing pleading, via electronic filing, through the U.S. District Court's ECF System to:

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On this the 6th day of June, 2011.

/s/ T. Robert Hill
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